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15 October 2014

Version of attached file:

Accepted Version

Peer-review status of attached file:

Peer-reviewed

Citation for published item:

Kuntz, J. and Safford, M.M. and Singh, J.A. and Phansalkar, S. and Slight, S.P. and Her, Q.L. and Lapointe, N.A. and Mathews, R. and O'Brien, E. and Brinkman, W.B. and Hommel, K. and Farmer, K.C. and Klinger, E. and Maniam, N. and Sobko, H.J. and Bailey, S.C. and Cho, I. and Rumptz, M.H. and Vandermeer, M.L. and Hornbrook, M.C. (2014) 'Patient-centered interventions to improve medication management and adherence : a qualitative review of research findings.', *Patient education and counseling*, 97 (3). pp. 310-326.

Further information on publisher's website:

<http://dx.doi.org/10.1016/j.pec.2014.08.021>

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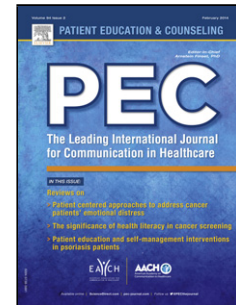
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Title: Patient-centered interventions to improve medication management and adherence: A qualitative review of research findings

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PII: S0738-3991(14)00371-1
DOI: <http://dx.doi.org/doi:10.1016/j.pec.2014.08.021>
Reference: PEC 4882

To appear in: *Patient Education and Counseling*

Received date: 21-2-2014
Revised date: 26-8-2014
Accepted date: 30-8-2014

Please cite this article as: Kuntz JL, Safford MM, Singh JA, Phansalkar S, Slight SP, Her QL, Lapointe NA, Mathews R, O'Brien E, Brinkman WB, Hommel K, Farmer KC, Klinger E, Maniam N, Sobko HJ, Bailey SC, Cho I, Rumptz MH, Vandermeer ML, Hornbrook MC, Patient-centered interventions to improve medication management and adherence: A qualitative review of research findings, *Patient Education and Counseling* (2014), <http://dx.doi.org/10.1016/j.pec.2014.08.021>

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Patient-centered interventions to improve medication management and adherence: a qualitative review of research findings

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Funding: This project was supported by grant number U19 HS021107 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality.

ABSTRACT

Objective: Patient-centered approaches to improving medication adherence hold promise, but evidence of their effectiveness is unclear. This review reports the current state of scientific research around interventions to improve medication management through four patient-centered domains: shared decision-making, methods to enhance effective prescribing, systems for eliciting and acting on patient feedback about medication use and treatment goals, and medication-taking behavior.

Methods: We reviewed literature on interventions that fell into these domains and were published between January 2007 and May 2013. Two reviewers abstracted information and categorized studies by intervention type.

Results: We identified 60 studies, of which 40% focused on patient education. Other intervention types included augmented pharmacy services, decision aids, shared decision-making, and clinical review of patient adherence. Medication adherence was an outcome in most (70%) of the studies, although 50% also examined patient-centered outcomes.

Conclusions: We identified a large number of medication management interventions that incorporated patient-centered care and improved patient outcomes. We were unable to determine whether these interventions are more effective than traditional medication adherence interventions.

Practice Implications: Additional research is needed to identify effective and feasible approaches to incorporate patient-centeredness into the medication management processes of the current health care system, if appropriate.

1. Introduction

Nearly 70% of Americans are prescribed at least one prescription drug, and 20% use five or more [1].

Medications have become a central component of the treatment of many diseases; however, 20% to 30% of prescriptions are never filled, and of those prescriptions that are filled, roughly half are not taken as prescribed [2]. These gaps in adherence result in an estimated \$100 billion to \$290 billion annually in avoidable health care costs [3-6]. Patients do not take prescribed medications for many reasons, including poor prescribing practices that create burdensome and complex regimens, concerns about cost and side effects, doubts about the benefit of medications, and low health literacy [7].

Interventions have attempted to increase medication adherence and related outcomes using a variety of approaches. Recent reviews of this literature found that the most effective medication adherence interventions adopted comprehensive approaches, involved several strategies, were high-intensity, and were tailored to individual patients [8-10]. However, these reviews also noted the low strength of evidence for many interventions and a need for more research to establish value and show improvements in health outcomes as a result of improved adherence [8-10]. Patient-centered approaches may represent a foundation upon which to develop new medication adherence interventions and enhance those that exist, but with the intent of also improving clinical outcomes, patient experience, and satisfaction with medication use.

The Agency for Healthcare Research and Quality (AHRQ)-funded Centers for Education and Research on Therapeutics (CERTs) program conducts research and provides education to advance the optimal use of drugs and medical devices, and biological products; increase awareness of the benefits and risks of therapeutics; and improve quality while cutting the costs of care. In 2012, the CERTs focused on how patient-centered care could be incorporated into efforts to improve medication management and

related outcomes among chronically ill patients. This initiative culminated in a workshop that brought together patients, providers, researchers, and other stakeholders to identify innovations, successes, and needs in the research and implementation of strategies to improve medication management through patient-centered approaches (McMullen, 2013, submitted in parallel – citation forthcoming). These approaches included four domains of the medication management process: shared decision-making, methods to enhance effective prescribing, systems for eliciting and acting on patient feedback about medication use and treatment goals, and support for medication-taking behavior (the traditional scope of adherence research). As part of this effort, we undertook a review of the literature to describe the current state of scientific research on patient-centered approaches to medication management. This paper summarizes the results of our review.

2. Methods

2.1. Design

2.1.1. Patient-centered medication management framework

This literature review outlined for attendees of the workshop the “state of the science” in patient-centered approaches to improving medication management. Prior to the workshop, drawing on the scientific literature and their own expertise, a steering group of CERTs researchers who have worked on adherence but have diverse backgrounds (medicine, pharmacy, informatics, epidemiology) as well as two patient representatives developed the “Patient-Centered Medication Management (PCMM)” framework to serve as the foundational concept to guide this literature review, as well as the workshop’s agenda and prioritization process. The PCMM framework sought to describe a process through which patient-centered care—defined as care that is respectful of and responsive to individual patient preferences, needs, and values and that ensures patient values guide all clinical decisions [11]—

is incorporated into practices that support medication prescribing and use. This framework outlined a number of activities related to medication management that included (1) shared decision-making, (2) methods to enhance effective prescribing, and (3) systems for eliciting and acting on patient feedback about medication-taking and treatment goals, and (4) medication-taking behavior.

Within the PCMM framework, **shared decision-making** refers to a process that results in decisions that are shared by providers and patients, informed by the best evidence available, and weighted according to the specific characteristics and values of the patient. The shared decision-making approach has been linked most frequently with therapeutic and screening decisions. However, in this context, shared decision-making refers to engaging the patient in prescribing decisions by communicating why a medication is indicated, its risks and benefits, and the likely impact on the patient's health.

Effective prescribing includes discussion of solutions to patients' perceived barriers to obtaining and taking medications that are part of an agreed-upon treatment plan. The ultimate goal of effective prescribing is to have the patient understand how and when the medication is to be taken.

Effective **patient feedback interventions** address unanticipated barriers and answer new questions that may come up as a patient proceeds with a prescribed treatment regimen. Effective feedback is facilitated by patient-provider communication, followed by an efficient process to modify the treatment plan if needed.

Medication-taking behavior interventions use effective (accessible, understandable, and useful) tools to inform patients and enhance accurate medication-taking, provide systems and resources that aid patients in obtaining medications in a timely and consistent manner, and offer options to help patients

with medication-taking at home. The medication-taking behavior component encompasses many of the interventions that address the traditional concept of medication adherence.

Collectively, these domains reflect the CERTs efforts to move beyond medication adherence and recognize the shift in perspective from the provider to the patient and the movement towards outcomes other than adherence that are important to patients. These include health outcomes, patient knowledge of and confidence in treatment regimens, patient satisfaction with care, and quality of patient-provider communication.

2.1.2. Search strategy

We performed a systematic search of publications describing the implementation and evaluation of interventions that incorporate at least one of the four PCMM domains (shared decision-making, effective prescribing, effective feedback, or medication-taking behavior) to improve medication management. Our search identified articles published in peer-reviewed medical journals between January 1, 2007, and May 31, 2013. We limited our search to the time period from 2007 forward to capture the current “state of the science” in patient-centered medication management. Searches were conducted using the Ovid MEDLINE and PubMed databases. We also scanned bibliographies of pertinent systematic and narrative reviews to identify relevant publications not captured by our search strategy [9;12].

Key words and phrases used in our search strategy are provided in Appendix 1. We used terms related to the type of study (e.g., “clinical trial,” “pretest,” “time series”), prescription drugs (e.g., “drug,” “medication,” “prescribing”), patient-centeredness (e.g., “patient preference,” “patient focused,” “shared decision-making”), and adherence (e.g., “adherence,” “compliance,” “medication adherence,”

“treatment adherence”). We used a Boolean approach to combine key words that indicated study type, outcomes, and a focus on medication use and patient-centered care. Search terms and parameters were adjusted for each database while maintaining a common overall structure. Search results were combined and screened for duplicate entries.

2.1.3. Selection of studies

We conducted an initial review of abstracts to determine their eligibility for full article review. We included articles in the full review if they described a randomized controlled trial, pragmatic trial, or quasi-experimental design that evaluated the implementation of an intervention to improve medication management and related outcomes through one of the PCMM framework components. We did not restrict studies by the type of outcome being measured; studies were not required to measure adherence as an outcome. Studies were English language only.

2.1.4. Data abstraction and synthesis

We created a data abstraction tool to collect a broad range of information, including intervention type, study design, clinical area, the health care provider who delivered the intervention, and measurement of outcomes. Two members of the research team independently applied our abstraction tool to articles that met the criteria for full review. A third reviewer resolved differences.

Our use of the PCMM framework as a guiding principle for this review allowed us to include a wide range of interventions targeting diverse outcomes. However, the framework domains were reflective of a continuous process for the management of prescribing and medication-taking and, thus, were overlapping. Therefore, although we could identify interventions based on the framework, we found it difficult to categorize interventions into mutually exclusive groups based on the framework. To account

for difficulty in the application of the framework and to provide structure to the discussion of results, interventions were categorized by the primary intervention type or approach through which researchers sought to impact the steps outlined in the PCMM framework. These intervention types were informed by the expertise of the steering group, are similar to intervention types reported in previous reviews of medication adherence interventions, and were collected as part of the abstraction process. We report interventions categorized into the following intervention types: (1) educational interventions, (2) augmented pharmacy services, (3) decision aids or shared decision-making, (4) case management, and (5) pharmacist or physician access to adherence or clinical outcome information and monitoring of medication-taking behaviors (i.e., feedback interventions).

We examined whether interventions focused on adherence, clinical, or patient-centered outcomes. Adherence measures varied widely, and included rates measured through prescription fills, pill counts, electronic monitoring, medication possession ratio (MPR), as well as self-report medication adherence scales. Clinical outcomes included measures that indicate a patient's disease status, such as cholesterol levels, depression symptom scores, or blood glucose levels. While alleviation of clinical symptoms, improvement in disease status, and successful adherence to medication regimens are clearly important to patients, for the purposes of this review, we defined a patient-centered outcome as an outcome of importance to patients but not inclusive of adherence or clinical measures (e.g., blood pressure). Examples of these outcomes included patient knowledge, quality of life, satisfaction, perceived control of symptoms, self-efficacy, understanding of treatment benefits and risks, and perceived barriers to medication use. We included hospitalization, mortality, and cost outcomes separately. We then qualitatively summarized the characteristics and outcomes of these interventions.

Although we collected data to describe the impact of interventions, study methodologies, outcome measurement, populations studied, and clinical focus, the studies were too heterogeneous to perform a formal meta-analysis. Thus, quantitative comparisons of effect sizes and discussion comparing study design and measurement methodology were outside the scope of this paper.

3. Results

3.1. Results of literature search

Using our search strategy, we identified 536 citations; manual searches of systematic reviews and other sources added 65 citations (Figure 1). After screening abstracts for eligibility and exclusion criteria, we reviewed 133 full-text articles. Following full-text review, 60 articles represented unique studies and were included. Of those, 43 were individual or cluster-randomized controlled trials, four were pragmatic trials, and 13 employed quasi-experimental study designs. Seven of the 13 quasi-experimental studies utilized a before-and-after design methodology, while the remaining six studies employed interrupted time series or other retrospective designs.

3.2. Description of Interventions and Impact on Outcomes

Interventions were categorized by the primary intervention type, as follows: (1) educational interventions delivered with or without additional behavioral or social support [13-28], through counseling [29-31], health coaching [32;33], or motivational interviewing [34;35], or in combination with feedback on clinical values, involving patients in self-monitoring, or e-health [36-38] (Table 1); (2) augmented pharmacy services [39-50] (Table 2); (3) decision aids or shared decision-making [51-59] (Table 3); (4) case management [60-67] (Table 4); and (5) feedback of adherence or clinical values to pharmacists or physicians or monitoring of medication-taking behaviors [68-72] (Table 4).

Interventions were delivered by a diverse group of professionals and, in many cases, more than one health care professional. Physicians, pharmacists, and multidisciplinary teams delivered interventions in 14, 12, and 11 studies, respectively. Physicians most often delivered decision aids, shared decision-making interventions, and educational interventions. Pharmacists were the only health care professionals to engage patients in augmented pharmacy services. The clinical conditions most frequently targeted by these interventions were cardiovascular diseases—including hypertension, atrial fibrillation, and heart failure. Other commonly targeted illnesses included diabetes and asthma. Time for patient follow-up after the intervention ranged from one-time measurements to five years, with a median duration of six months.

Nearly all of the studies evaluated the impact of the intervention on more than one outcome, although medication adherence was assessed most commonly, in 43 of the 60 studies. Studies also focused on patient-centered outcomes such as quality of life, patient knowledge, and patient satisfaction (34 studies); clinical outcomes including measures of disease status such as blood pressure, cholesterol levels, and depression symptom scores (26 studies); hospitalization or mortality outcomes (nine studies); and medication utilization (eight studies) or cost to patients or health plans (five studies).

3.2.1. Patient education interventions

Educational interventions provided information to patients about already prescribed medication regimens and often resulted in better medication adherence and greater patient knowledge. The benefits of these interventions were most evident in their impact on patient-centered outcomes such as patient knowledge, self-efficacy, and self-monitoring skills. The most successful educational

interventions combined patient education with efforts such as coaching or behavioral and social support.

Twenty-six of the 60 studies reported on educational interventions, with or without additional components such as behavioral or social support (Table 1). The majority of these interventions (16 of 26 studies) focused on medication-taking [13;17-20;23-28;30;31;34;36;37], while five addressed effective prescribing [16;22;29;35;38], four utilized shared decision-making [14;15;32;33], and one addressed effective feedback [21]. Educational interventions were frequently delivered by research personnel or multidisciplinary teams. These interventions were commonly repetitive and occurred over varied periods of time, ranging from weeks to years, making comparison difficult.

Sixteen of the 26 educational intervention studies examined medication adherence as an outcome. Patients receiving education typically had higher adherence rates than patients receiving usual care. However, in a number of studies, the intervention produced no significant long-term impact on adherence when compared to patients not receiving the intervention [19;23;25;31;35]. For example, Pladevall et al. reported a 30% increase in medication adherence following education supplemented by adherence monitoring and provision of social support, although the control group also improved adherence by 20% and both groups attained approximately 90% adherence upon study completion [25]. Several studies reported diminishing adherence rates over study follow-up. For example, in one study, patients who participated in group educational meetings had a 26% decrease in adherence over the course of study follow-up. However, in the same study, patients who received education on an individual basis experienced a similar 25% decline in adherence [14]. In fact, a number of studies noted that significantly higher adherence rates among intervention versus control patients were attributed only to a slower decline in adherence over time among intervention patients [14;23;24;27;31].

Patient-centered outcomes were measured in 14 educational interventions, with 11 studies reporting significant improvements in one or more of these outcomes. Four studies reported adherence improvements as well as increased patient knowledge, self-efficacy, and self-monitoring skills; reductions in barriers to adherence; and greater patient activation [20;24;27;33]. Notably, for these outcomes, successful interventions combined patient education with supplemental coaching, motivational approaches, or social support.

Seven of the nine educational intervention studies that measured clinical outcomes found significant improvements in the management of diabetes [13;33;35], hypertension [17;25], mental health among rheumatoid arthritis patients [26], and fracture risk among osteoporosis patients [37]. Two studies examined hospitalization among hypertensive patients; one of these studies resulted in decreased hospitalization [21], while one did not [19], despite having interventions that were relatively similar in intensity. Finally, only one of four studies to examine mortality outcomes found a significant survival benefit [28].

Six studies provided insight into resource investment and patient selection associated with educational interventions. Homer et al. found that the provision of information in group settings rather than on an individual basis led to better adherence and lower rates of drug discontinuation, while using fewer health care resources and incurring lower costs to patients and health plans [14]. In other studies, authors noted that educational interventions might be most cost-effective among less-adherent populations [19] and most effective in improving outcomes among patients with an acute event [13], patients with a shorter time since diagnosis and initial prescribing [26], patients with high health literacy [26], and patients who are “ready for change” [33;37]. However, the lack of consistency among the

studies in design and measures limits the ability to draw general conclusions about subgroup-specific effectiveness and cost savings.

3.2.2. Augmented pharmacy services interventions

Augmented pharmacy services studies commonly targeted medically complex patients, identified barriers to already prescribed medication use, and documented effects on outcomes after initial treatment decisions were made. The benefits of these interventions were most evident in the tailoring of medication regimens to ongoing patient needs and in cost reduction. Many pharmacy interventions were tailored to specific patient needs and delivered by pharmacy staff on a one-on-one basis; however, patient-centered outcomes were rarely measured.

Augmented pharmacy services interventions primarily targeted elderly patients with multiple comorbid conditions who were taking several medications (Table 2). The majority of these interventions (eight of 12 studies) focused on medication-taking [39;41;44-46;49;50], while three addressed effective prescribing [42;47;48] and two centered on effective feedback [40;43]. Generally, these interventions were delivered by pharmacists or pharmacy staff and provided tailored information and tools to patients that allowed for adjustment of regimens to match patient needs. Interventions commonly involved multiple avenues for interaction with patients, including face-to-face and telephone encounters. Although the majority of these interventions included populations with complex medication needs, a number of interventions focused on specific chronic conditions [41;42;45-47;50] or specific medications [41].

Evidence supporting the interventions' effectiveness in improving medication adherence was mixed, although significant positive changes [41;45-48;50] were observed more often than negative or non-

significant findings [39;42]. Patient-centered outcomes were less likely to be measured than clinical or adherence outcomes following pharmacy interventions; however, when assessed, patients were often satisfied with their interactions with pharmacists and with potential cost savings. Overall, patient cost and utilization outcomes were measured following augmented pharmacy services more frequently than for any other type of intervention. There appeared to be a trend toward reduced costs to patients [39;44;47;48;50]; however, Welch et al. reported *increased* medication costs following a medication review and counseling intervention [49]. Welch et al. noted that addressing important safety issues such as drug-drug interactions, identification of medication gaps, and under-treatment resulted in improvements in medication regimens and patient adherence; however, patient costs also increased [49]. In contrast, Pindolia et al. reported reductions in total prescriptions per patient per month and reduced pharmacy costs after implementing an intervention that invested only 2.5 hours of telephone contact per patient [48]. Longer-term costs may have been lowered through improved treatment but were not assessed in these studies.

3.2.3. Decision aids and shared decision-making interventions

We found that decision-making interventions most closely fit the paradigm of patient-centered care. These interventions were implemented at the time of prescribing and often resulted in increased patient knowledge, although there was little evidence for impact on ongoing decision-making or improvements in adherence or clinical outcomes.

Nine studies employed decision aids or shared decision-making (SDM) as the principal component of their interventions (Table 3). [51-59]. These interventions were most often delivered by physicians during face-to-face health care encounters and were designed to provide patients with information about potential treatment choices and their associated benefits and risks.

Decision aid and SDM interventions are typically designed to inform choice rather than change behavior [55;58]. Accordingly, the measurement of patient knowledge was common (eight of the nine studies) and improvements were noted in seven studies [51-56;58]. Three studies measured and showed improvements in patient participation, confidence in decision-making, and satisfaction with care [53;54;56]. Three studies reported that patients' understanding of risk was improved and decisional conflict lessened [52;54;55]. However, authors observed that increased patient knowledge did not change the patient decision-making process, and there was little evidence that treatment choice or patient beliefs changed even when patients were more informed about benefits and risks [52-55;57;58]. This suggests that patients may have a wide range of considerations when making treatment decisions, not just medical facts; however, these studies did not report on the range of considerations or the basis for patient decision-making. For example, Thomson et al. found that patient uptake of warfarin actually decreased despite a reduction in decisional conflict [52], although the study did not report the patient perspective on what led to this outcome. Two of the four studies in this category that sought to increase medication adherence resulted in improvements [51;54]. Only one of the three studies that sought to improve clinical outcomes identified improvements [51]. In fact, Montori et al. noted that there is little evidence that decision aids improve adherence, and concurrently, that there is limited opportunity to improve clinical outcomes following decision aid use [54].

3.2.4. Case management interventions

Case management interventions commonly employed individualized assessments of patient barriers to medication-taking and tailored approaches to address these barriers. However, the limited number of studies and the wide variation in both the approaches used and resources dedicated to these interventions make it difficult to draw any conclusions about overall effectiveness.

In eight case management intervention studies (Table 4), nurses and care teams delivered the intervention. Four of eight studies focused on medication-taking [60;61;66;67], three studies focused on effective feedback [62-64], and one focused on effective prescribing [65]. Case management interventions targeted patients with a wide variety of clinical conditions. All studies that measured adherence found either significant improvement in adherence among patients who received the intervention [60-62;65;67]. In addition, four of eight case management studies examined clinical outcomes; all four of these resulted in significant improvements [60;61;64;66]. Last, two case management studies measured quality of life and found no effect [60;63].

3.2.5. Feedback interventions

These interventions intended to utilize feedback to foster further discussion of current treatment regimen with the patient as a means to inform changes to these regimens. Five studies provided pharmacists or physicians with information regarding patient medication adherence and clinical status through health information technology, direct patient report, or medical record review (Table 4). Of these interventions, two focused on effective feedback [68;71], two concentrated on medication-taking behavior [70;73], and one centered on effective prescribing [69]. Interventions employing feedback and access to medication adherence information were most commonly conducted among patients with hypertension [70;71] or patients undergoing care for psychiatric illness or depression [68;69;72]. Two of the five studies showed an increase in patient satisfaction regarding care and concordance between patient preferences and prescribed regimens [69;72]. Wilder et al. found that psychiatric patients were more likely to adhere to medications if they received treatments that they preferred, thus underlining the importance of patient preference in medication decision-making and effectiveness [69].

4. Discussion and Conclusion

4.1. Discussion

Our review describes the extent to which current medication management interventions incorporate elements of patient-centeredness. Our use of the PCMM framework as a guiding principle allowed us to include a wide range of interventions targeting diverse outcomes. However, we found it difficult to meaningfully and consistently categorize interventions into mutually exclusive groups based on the framework's domains, because they are overlapping: shared decision-making, effective prescribing, effective feedback, and medication-taking behavior. This suggests that our framework may better serve as a template for improving how providers and patients engage in medication management than as a structure for studying this process in the scientific literature. In addition, the studies were heterogeneous and results were difficult to collectively interpret. Thus, we could not draw firm conclusions as to whether patient-centered medication management interventions represent a distinct shift away from or an improvement over more traditional medication adherence interventions. Rather, we provide a broad description of interventions, the approaches they took to engage patients, and their contribution to the improvement of outcomes, with the intent of informing the development of future efforts.

A number of comprehensive reviews of medication adherence interventions have been published. A recent evidence review found that a variety of interventions led to adherence improvements, with interventions to reduce out-of-pocket expenses, case management, and educational interventions the most effective across clinical conditions [8]. The authors noted that the majority of efforts to improve adherence did not examine patient-reported outcomes, and when better adherence was observed, there was little evidence of improvement in patients' health outcomes [8]. Our review generally supports this view.

Our review was different from previous reviews because we focused on patient engagement and patient-centered approaches, allowed for observational study designs, and included patient-centered outcomes. Patient knowledge, patient satisfaction, and quality-of-life outcomes were the most commonly-included patient-centered outcomes and were measured in 34 of the 60 articles reviewed. However, additional concepts central to the process of patient-centered care, such as preference for treatment regimens and patients' health care goals, were rarely reported. This may be due to difficulties in measuring these processes and outcomes, such as the lack of widely applied and validated methods. Although all of the included interventions were deemed to be patient-centered, the most common focus was still medication adherence. A variety of interventions observed improvements in adherence over the follow-up period; however, since average follow-up was less than one year, we do not know the optimal length of time over which an intervention should be implemented or the sustainability of intervention effects over time. In turn, there were inconsistent results for a link between adherence and clinical outcomes improvement.

Interventions were delivered by a diverse group of health care providers, either by individuals or as part of collaborative or coordinated care. Many interventions were carried out at one level within a health care visit or setting (e.g., augmented pharmacy services, decision aids, or shared decision-making interventions), despite recognition of the importance of collaborative or coordinated care in the medication adherence literature. For interventions that did incorporate collaborative care, the participation of personnel not otherwise present in the health care system (e.g., study personnel) was common, thus limiting their generalizability.

We found that many studies included small patient samples with very specific clinical and therapeutic needs. Small sample sizes may be due to the high level of tailoring required or the difficulty in systematically developing and carrying out individualized interventions. Furthermore, with the exception of augmented pharmacy services interventions, patients with complex medication needs were often excluded, reducing the potential “real-world” applicability. In addition, many efforts were likely expensive, although details of cost and time commitment were not commonly reported; in most cases, the impact on health care-provider time and the complexity of coordination would also limit generalizability. Finally, interventions were implemented with a focus on specific aspects of medication management; studies did not typically address medication management starting at the prescribing decision and extending to appropriate medication-taking behavior. Thus, combinations of these interventions may be needed to provide long-term impacts on patient outcomes.

Our review has a number of limitations. We based our literature search on our PCMM framework, which was informed by the Institute of Medicine’s definition of patient-centered care. We also identified previously published reviews and search strategies that attempted to ascertain patient-centeredness within the scientific literature. Despite these efforts, since the concept of patient-centered care is relatively new and continuously evolving, we may have missed relevant articles.

In addition, we included studies from different populations and clinical settings, with different disease emphases, and differing methodology and measurement. Thus, quantitative comparisons of effect sizes and discussion comparing study design and measurement methodology were outside the scope of this paper. Finally, our summary may suffer from publication or reporting bias, as we found few articles that reported negative results for all outcomes measured.

4.2. Conclusions

Our review identified efforts to involve patients in medication prescribing and use. Evidence supporting overall effectiveness of interventions was sparse. Furthermore, there was limited evidence of improved patient-centered outcomes or clinical endpoints and sustained improvement in outcomes. Variability in the delivery of interventions and outcomes measured precluded concrete comparisons between interventions or comparisons with traditional medication adherence interventions. In general, it is not clear that patient-centered medication management interventions represent an improvement over more traditional medication adherence interventions.

4.3 Practice Implications and future research

Additional research is needed to examine how to integrate patient-centered care into medication management. This requires the development of definitions and methods to standardize the measurement of adherence and patient-centered outcomes, to allow for comparisons of interventions. Also, future study teams may want to consider incorporating qualitative research methods to provide detail regarding how patient-centered care is delivered and how patient-centeredness is perceived and received by patients. Finally, we encourage additional research within different populations with different clinical needs, that **assesses** the effectiveness of specific intervention types as well as combinations of intervention types, and that **assesses** the resources needed to address both initial and chronic medication management issues. These efforts would help foster the identification of effective and feasible approaches to incorporate patient-centeredness into the medication management processes of the current health care system, if appropriate.

Author statement

I confirm that all authors have read this manuscript and given their permission for it to be published in PEC.

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Reference List

- [1] Zhong W, Maradit-Kremers H, St Sauver JL, Yawn BP, Ebbert JO, Roger VL, Jacobson DJ, McGree ME, Brue SM, Rocca WA. Age and sex patterns of drug prescribing in a defined american population. *Mayo Clin Proc* 2013 Jul;88:697-707.
- [2] Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence. *Am J Health Syst Pharm* 2003 Apr 1;60:657-65.
- [3] New England Healthcare Institute. Thinking Outside the Pillbox. Retrieved from: http://www.nehi.net/publications/44/thinking_outside_the_pillbox_a_systemwide_approach_to_improving_patient_medication_adherence_for_chronic_disease
- [4] Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care* 2005 Jun;43:521-30.
- [5] Roebuck MC, Liberman JN, Gemmill-Toyama M, Brennan TA. Medication adherence leads to lower health care use and costs despite increased drug spending. *Health Aff (Millwood)* 2011 Jan;30:91-9.
- [6] DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. *Med Care* 2002 Sep;40:794-811.
- [7] Briesacher BA, Gurwitz JH, Soumerai SB. Patients at-risk for cost-related medication nonadherence: a review of the literature. *J Gen Intern Med* 2007 Jun;22:864-71.
- [8] Medication Adherence Interventions: Comparative Effectiveness. Closing the Quality Gap: Revisiting the State of the Science. Evidence Report No. 208. (Prepared by RTI International-University of North Carolina Evidence-based Practice Center under Contract No. 290-2007-10056-I.) AHRQ Publication No. 12-E010-EF. Viswanathan M, Golin C, Jones C, Ashlok M, Blalock S, Wines R, Coker-Schwimmer E, Grodensky C, Rosen D, Yuen A, Sista P, Lohr K. 2012 Sep.
- [9] Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock SJ, Wines RC, Coker-Schwimmer EJ, Rosen DL, Sista P, Lohr KN. Interventions to improve adherence to self-administered medications for chronic diseases in the United States: a systematic review. *Ann Intern Med* 2012 Dec 4;157:785-95.
- [10] Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2008;CD000011.
- [11] Committee on Quality of Health Care in America IoM. Crossing the Quality Chasm: A New Health System for the 21st Century. The National Academies Press; 2001.
- [12] Stacey D, Bennett CL, Barry MJ, Col NF, Eden KB, Holmes-Rovner M, Llewellyn-Thomas H, Lyddiatt A, Legare F, Thomson R. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev* 2011;CD001431.

- [13] Pearce KA, Love MM, Shelton BJ, Schoenberg NE, Williamson MA, Barron MA, Houlihan JM. Cardiovascular risk education and social support (CaRESS): report of a randomized controlled trial from the Kentucky Ambulatory Network (KAN). *J Am Board Fam Med* 2008 Jul;21:269-81.
- [14] Homer D, Nightingale P, Jobanputra P. Providing patients with information about disease-modifying anti-rheumatic drugs: Individually or in groups? A pilot randomized controlled trial comparing adherence and satisfaction. *Musculoskeletal Care* 2009 Jun;7:78-92.
- [15] Park J, Jackson J, Skinner E, Ranghell K, Saiers J, Cherney B. Impact of an adherence intervention program on medication adherence barriers, asthma control, and productivity/daily activities in patients with asthma. *Journal of Asthma* 2010 Dec;47:1072-7.
- [16] McCarthy ML, Ding R, Roderer NK, Steinwachs DM, Ortmann MJ, Pham JC, Bessman ES, Kelen GD, Atha W, Retezar R, Bessman SC, Zeger SL. Does Providing Prescription Information or Services Improve Medication Adherence Among Patients Discharged From the Emergency Department? A Randomized Controlled Trial. *Ann Emerg Med* 2013 Apr 2.
- [17] Hacıhasanoglu R, Gozum S. The effect of patient education and home monitoring on medication compliance, hypertension management, healthy lifestyle behaviours and BMI in a primary health care setting. *Journal of Clinical Nursing* 2011 Mar;20:692-705.
- [18] Grosset KA, Grosset DG. Effect of educational intervention on medication timing in Parkinson's disease: a randomized controlled trial. *BMC Neurol* 2007;7:20.
- [19] Edworthy SM, Baptie B, Galvin D, Brant RF, Churchill-Smith T, Manyari D, Belenkie I. Effects of an enhanced secondary prevention program for patients with heart disease: a prospective randomized trial. *Can J Cardiol* 2007 Nov;23:1066-72.
- [20] Chen SY, Sheu S, Chang CS, Wang TH, Huang MS. The effects of the self-efficacy method on adult asthmatic patient self-care behavior. *J Nurs Res* 2010 Dec;18:266-74.
- [21] Bocchi EA, Cruz F, Guimaraes G, Pinho Moreira LF, Issa VS, Ayub Ferreira SM, Chizzola PR, Souza GE, Brandao S, Bacal F. Long-term prospective, randomized, controlled study using repetitive education at six-month intervals and monitoring for adherence in heart failure outpatients: the REMADHE trial. *Circ Heart Fail* 2008 Jul;1:115-24.
- [22] Altiner A, Brockmann S, Sielk M, Wilm S, Wegscheider K, Abholz HH. Reducing antibiotic prescriptions for acute cough by motivating GPs to change their attitudes to communication and empowering patients: a cluster-randomized intervention study. *Journal of Antimicrobial Chemotherapy* 2007 Sep;60:638-44.
- [23] Janson SL, McGrath KW, Covington JK, Cheng SC, Boushey HA. Individualized asthma self-management improves medication adherence and markers of asthma control. *J Allergy Clin Immunol* 2009 Apr;123:840-6.
- [24] Nielsen D, Ryg J, Nielsen W, Knold B, Nissen N, Brixen K. Patient education in groups increases knowledge of osteoporosis and adherence to treatment: a two-year randomized controlled trial. *Patient Educ Couns* 2010 Nov;81:155-60.

- [25] Pladevall M, Brotons C, Gabriel R, Arnau A, Suarez C, de la Figuera M, Marquez E, Coca A, Sobrino J, Divine G, Heisler M, Williams LK. Multicenter cluster-randomized trial of a multifactorial intervention to improve antihypertensive medication adherence and blood pressure control among patients at high cardiovascular risk (the COM99 study). *Circulation* 2010 Sep 21;122:1183-91.
- [26] Rudd RE, Blanch DC, Gall V, Chibnik LB, Wright EA, Reichmann W, Liang MH, Katz JN. A randomized controlled trial of an intervention to reduce low literacy barriers in inflammatory arthritis management. *Patient Educ Couns* 2009 Jun;75:334-9.
- [27] Moshkovska T, Stone MA, Smith RM, Bankart J, Baker R, Mayberry JF. Impact of a tailored patient preference intervention in adherence to 5-aminosalicylic acid medication in ulcerative colitis: results from an exploratory randomized controlled trial. *Inflammatory Bowel Diseases* 2011 Sep;17:1874-81.
- [28] Wu JR, Corley DJ, Lennie TA, Moser DK. Effect of a medication-taking behavior feedback theory-based intervention on outcomes in patients with heart failure. *J Card Fail* 2012 Jan;18:1-9.
- [29] Adie K, James MA. Does telephone follow-up improve blood pressure after minor stroke or TIA? *Age & Ageing* 2010 Sep;39:598-603.
- [30] Perahia DG, Quail D, Gandhi P, Walker DJ, Peveler RC. A randomized, controlled trial of duloxetine alone vs. duloxetine plus a telephone intervention in the treatment of depression. *J Affect Disord* 2008 May;108:33-41.
- [31] Taitel M, Jiang J, Rudkin K, Ewing S, Duncan I. The impact of pharmacist face-to-face counseling to improve medication adherence among patients initiating statin therapy. *Patient preference & adherence* 2012;6:323-9.
- [32] Ho EY, D'Agostino TA, Yadegar V, Burke A, Bylund CL. Teaching patients how to talk with biomedical providers about their complementary and alternative medicine use. *Patient Educ Couns* 2012 Dec;89:405-10.
- [33] Wolever RQ, Dreusicke M, Fikkan J, Hawkins TV, Yeung S, Wakefield J, Duda L, Flowers P, Cook C, Skinner E. Integrative health coaching for patients with type 2 diabetes: a randomized clinical trial. *Diabetes Educ* 2010 Jul;36:629-39.
- [34] Finocchiaro-Kessler S, Catley D, Thomson D, Bradley-Ewing A, Berkley-Patton J, Goggin K. Patient communication tools to enhance ART adherence counseling in low and high resource settings. *Patient Educ Couns* 2012 Oct;89:163-70.
- [35] Rubak S, Sandbaek A, Lauritzen T, Borch-Johnsen K, Christensen B. Effect of "motivational interviewing" on quality of care measures in screen detected type 2 diabetes patients: a one-year follow-up of an RCT, ADDITION Denmark. *Scand J Prim Health Care* 2011 Jun;29:92-8.
- [36] Neafsey PJ, M'lan CE, Ge M, Walsh SJ, Lin CA, Anderson E. Reducing Adverse Self-Medication Behaviors in Older Adults with Hypertension: Results of an e-health Clinical Efficacy Trial. *Ageing Int* 2011 Jun;36:159-91.

- [37] Delmas PD, Vrijens B, Eastell R, Roux C, Pols HA, Ringe JD, Grauer A, Cahall D, Watts NB. Effect of monitoring bone turnover markers on persistence with risedronate treatment of postmenopausal osteoporosis. *J Clin Endocrinol Metab* 2007 Apr;92:1296-304.
- [38] Nassaralla CL, Naessens JM, Hunt VL, Bhagra A, Chaudhry R, Hansen MA, Tulledge-Scheitel SM. Medication reconciliation in ambulatory care: attempts at improvement. *Quality & Safety in Health Care* 2009 Oct;18:402-7.
- [39] Shimp LA, Kucukarslan SN, Elder J, Remington T, Wells T, Choe HM, Lewis NJ, Kirking DM. Employer-based patient-centered medication therapy management program: evidence and recommendations for future programs. *Journal of the American Pharmacists Association: JAPhA* 2012 Nov;52:768-76.
- [40] Calvert SB, Kramer JM, Anstrom KJ, Kaltenbach LA, Stafford JA, Allen LaPointe NM. Patient-focused intervention to improve long-term adherence to evidence-based medications: a randomized trial. *American Heart Journal* 2012 Apr;163:657-65.
- [41] Eussen SR, van der Elst ME, Klungel OH, Rompelberg CJ, Garssen J, Oosterveld MH, de BA, de Gier JJ, Bouvy ML. A pharmaceutical care program to improve adherence to statin therapy: a randomized controlled trial. *Ann Pharmacother* 2010 Dec;44:1905-13.
- [42] Hunt JS, Siemieniczuk J, Pape G, Rozenfeld Y, MacKay J, LeBlanc BH, Touchette D. A randomized controlled trial of team-based care: impact of physician-pharmacist collaboration on uncontrolled hypertension. *J Gen Intern Med* 2008 Dec;23:1966-72.
- [43] Lenaghan E, Holland R, Brooks A. Home-based medication review in a high risk elderly population in primary care--the POLYMED randomised controlled trial. *Age Ageing* 2007 May;36:292-7.
- [44] Elliott RA, Barber N, Clifford S, Horne R, Hartley E. The cost effectiveness of a telephone-based pharmacy advisory service to improve adherence to newly prescribed medicines. *Pharmacy World & Science* 2008 Jan;30:17-23.
- [45] Phumipamorn S, Pongwecharak J, Soorapan S, Pattharachayakul S. Effects of the pharmacist's input on glycaemic control and cardiovascular risks in Muslim diabetes. *Prim Care Diabetes* 2008 Feb;2:31-7.
- [46] Klein A, Otto G, Kramer I. Impact of a pharmaceutical care program on liver transplant patients' compliance with immunosuppressive medication: a prospective, randomized, controlled trial using electronic monitoring. *Transplantation* 2009 Mar 27;87:839-47.
- [47] Monte SV, Slazak EM, Albanese NP, Adelman M, Rao G, Paladino JA. Clinical and economic impact of a diabetes clinical pharmacy service program in a university and primary care-based collaboration model. *Journal of the American Pharmacists Association: JAPhA* 2009 Mar;49:200-8.
- [48] Pindolia VK, Stebelsky L, Romain TM, Luoma L, Nowak SN, Gillanders F. Mitigation of medication mishaps via medication therapy management. *Annals of Pharmacotherapy* 2009 Apr;43:611-20.

- [49] Welch EK, Delate T, Chester EA, Stubbings T. Assessment of the impact of medication therapy management delivered to home-based Medicare beneficiaries. *Annals of Pharmacotherapy* 2009 Apr;43:603-10.
- [50] Moore JM, Shartle D, Faudskar L, Matlin OS, Brennan TA. Impact of a patient-centered pharmacy program and intervention in a high-risk group. *Journal of Managed Care Pharmacy* 2013 Apr;19:228-36.
- [51] Wilson SR, Strub P, Buist AS, Knowles SB, Lavori PW, Lapidus J, Vollmer WM. Shared treatment decision making improves adherence and outcomes in poorly controlled asthma. *Am J Respir Crit Care Med* 2010 Mar 15;181:566-77.
- [52] Thomson RG, Eccles MP, Steen IN, Greenaway J, Stobbart L, Murtagh MJ, May CR. A patient decision aid to support shared decision-making on anti-thrombotic treatment of patients with atrial fibrillation: randomised controlled trial. *Qual Saf Health Care* 2007 Jun;16:216-23.
- [53] Mullan RJ, Montori VM, Shah ND, Christianson TJ, Bryant SC, Guyatt GH, Perestelo-Perez LI, Stroebe RJ, Yawn BP, Yapuncich V, Breslin MA, Pencille L, Smith SA. The diabetes mellitus medication choice decision aid: a randomized trial. *Archives of Internal Medicine* 2009 Sep 28;169:1560-8.
- [54] Montori VM, Shah ND, Pencille LJ, Branda ME, Van Houten HK, Swiglo BA, Kesman RL, Tulledge-Scheitel SM, Jaeger TM, Johnson RE, Bartel GA, Melton LJ, III, Wermers RA. Use of a decision aid to improve treatment decisions in osteoporosis: the osteoporosis choice randomized trial. *American Journal of Medicine* 2011 Jun;124:549-56.
- [55] Mann DM, Ponienman D, Montori VM, Arciniega J, McGinn T. The Statin Choice decision aid in primary care: a randomized trial. *Patient Education & Counseling* 2010 Jul;80:138-40.
- [56] Loh A, Simon D, Wills CE, Kriston L, Niebling W, Harter M. The effects of a shared decision-making intervention in primary care of depression: a cluster-randomized controlled trial. *Patient Educ Couns* 2007 Aug;67:324-32.
- [57] Kasper J, Kopke S, Muhlhauser I, Nubling M, Heesen C. Informed shared decision making about immunotherapy for patients with multiple sclerosis (ISDIMS): a randomized controlled trial. *Eur J Neurol* 2008 Dec;15:1345-52.
- [58] Fagerlin A, Zikmund-Fisher BJ, Nair V, Derry HA, McClure JB, Greene S, Stark A, Hensley AS, Lantz P, Hayes DF, Wiese C, Claud ZS, Pitsch R, Jankovic A, Ubel PA. Women's decisions regarding tamoxifen for breast cancer prevention: responses to a tailored decision aid. *Breast Cancer Res Treat* 2010 Feb;119:613-20.
- [59] Deinzer A, Veelken R, Kohnen R, Schmieder RE. Is a shared decision-making approach effective in improving hypertension management? *J Clin Hypertens (Greenwich)* 2009 May;11:266-70.
- [60] Gensichen J, von KM, Peitz M, Muth C, Beyer M, Guthlin C, Torge M, Petersen JJ, Rosemann T, Konig J, Gerlach FM. Case management for depression by health care assistants in small primary care practices: a cluster randomized trial. *Ann Intern Med* 2009 Sep 15;151:369-78.

- [61] Bogner HR, Morales KH, de Vries HF, Cappola AR. Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. *Ann Fam Med* 2012 Jan;10:15-22.
- [62] Hudson TJ, Owen RR, Thrush CR, Armitage TL, Thapa P. Guideline implementation and patient-tailoring strategies to improve medication adherence for schizophrenia. *Journal of Clinical Psychiatry* 2008 Jan;69:74-80.
- [63] Olsson IN, Runnamo R, Engfeldt P. Drug treatment in the elderly: an intervention in primary care to enhance prescription quality and quality of life. *Scandinavian Journal of Primary Health Care* 2012 Mar;30:3-9.
- [64] Wakefield BJ, Holman JE, Ray A, Scherubel M, Adams MR, Hillis SL, Rosenthal GE. Effectiveness of home telehealth in comorbid diabetes and hypertension: a randomized, controlled trial. *Telemed J E Health* 2011 May;17:254-61.
- [65] Stanhope V, Ingoglia C, Schmelter B, Marcus SC. Impact of person-centered planning and collaborative documentation on treatment adherence. *Psychiatric Services* 2013 Jan;64:76-9.
- [66] Chimbanrai B, Fungladda W, Kaewkungwal J, Silachamroon U. Treatment-seeking behaviors and improvement in adherence to treatment regimen of tuberculosis patients using intensive triad-model program, Thailand. *Southeast Asian Journal of Tropical Medicine & Public Health* 2008 May;39:526-41.
- [67] Gelmanova IY, Taran DV, Mishustin SP, Golubkov AA, Solovyova AV, Keshavjee S. 'Sputnik': a programmatic approach to improve tuberculosis treatment adherence and outcome among defaulters. *International Journal of Tuberculosis & Lung Disease* 2011 Oct;15:1373-9.
- [68] Chang TE, Jing Y, Yeung AS, Brennenman SK, Kalsekar I, Hebden T, McQuade R, Baer L, Kurlander JL, Watkins AK, Siebenaler JA, Fava M. Effect of communicating depression severity on physician prescribing patterns: findings from the Clinical Outcomes in MEasurement-based Treatment (COMET) trial. *General Hospital Psychiatry* 2012 Mar;34:105-12.
- [69] Wilder CM, Elbogen EB, Moser LL, Swanson JW, Swartz MS. Medication preferences and adherence among individuals with severe mental illness and psychiatric advance directives. *Psychiatric Services* 2010 Apr;61:380-5.
- [70] Christensen A, Christrup LL, Fabricius PE, Chrostowska M, Wronka M, Narkiewicz K, Hansen EH. The impact of an electronic monitoring and reminder device on patient compliance with antihypertensive therapy: a randomized controlled trial. *J Hypertens* 2010 Jan;28:194-200.
- [71] Rinfret S, Lussier MT, Peirce A, Duhamel F, Cossette S, Lalonde L, Tremblay C, Guertin MC, LeLorier J, Turgeon J, Hamet P. The impact of a multidisciplinary information technology-supported program on blood pressure control in primary care. *Circ Cardiovasc Qual Outcomes* 2009 May;2:170-7.
- [72] Simon GE, Ralston JD, Savarino J, Pabiniak C, Wentzel C, Operskalski BH. Randomized trial of depression follow-up care by online messaging. *Journal of General Internal Medicine* 2011 Jul;26:698-704.

- [73] Simon SR, Smith DH, Feldstein AC, Perrin N, Yang X, Zhou Y, Platt R, Soumerai SB. Computerized prescribing alerts and group academic detailing to reduce the use of potentially inappropriate medications in older people. *J Am Geriatr Soc* 2006 Jun;54:963-8.

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Figure 1. Study selection criteria and flow diagram.

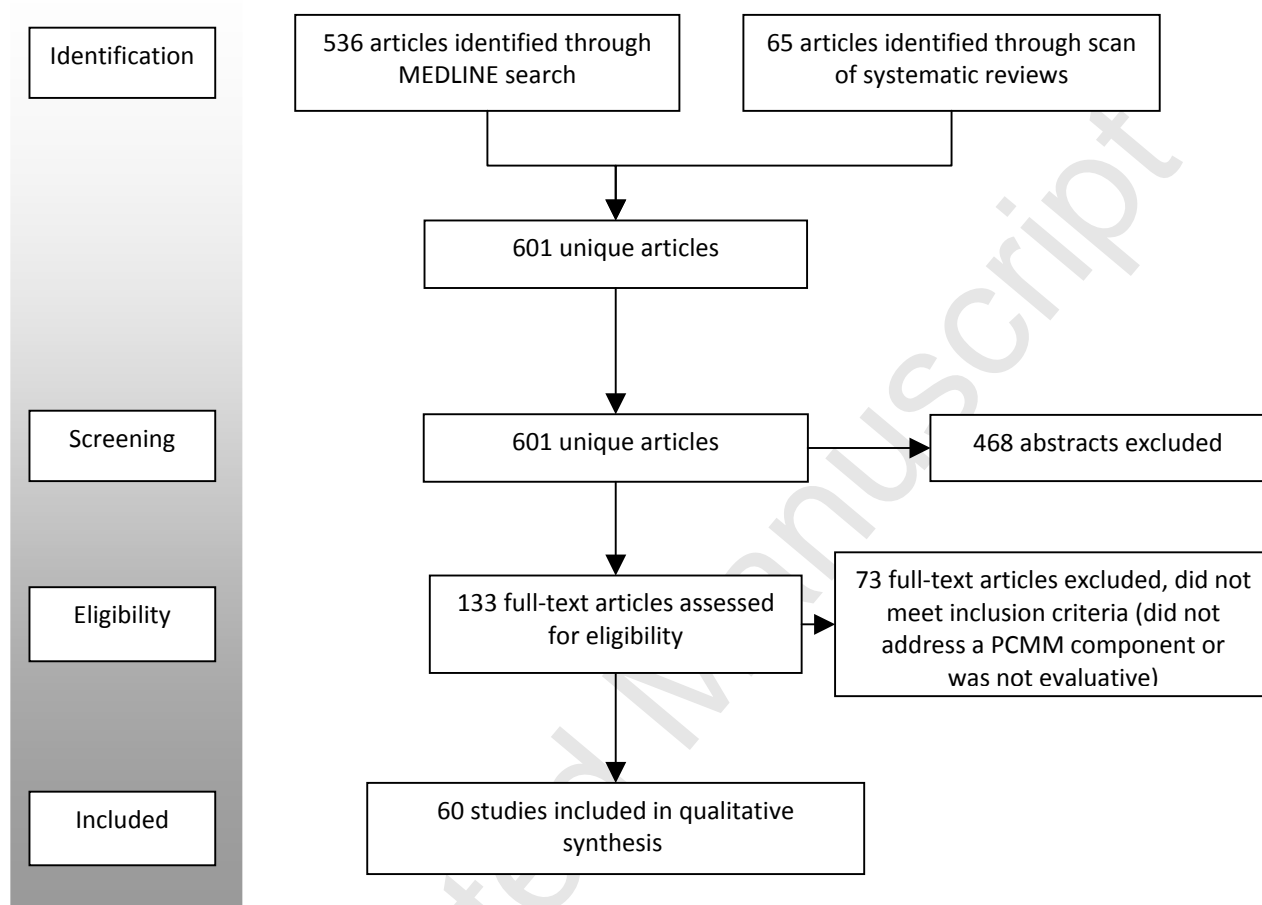


Table 1. Educational interventions to improve patient-centered medication management.

Study	Intervention Description	Clinical area	Intervention agent	Duration of follow-up	Evidence for medication adherence outcomes	Evidence for non-adherence outcomes
Education						
Altiner 2007	Education to address physician-patient misunderstandings and empower patients	Outpatient antibiotics	Physician	6 weeks; 12 months	NA	Rate of antibiotic prescribing: Decrease (+)
Grosset 2007	Patient education about continuous dopaminergic therapy	Parkinson's Disease	Researcher	3 months	IG: 17% timing adherence at baseline increased to 39% CG: 21% timing adherence increased to 20% (p=0.007) The difference in timing adherence pre- to post-intervention between the 2 groups was 13.4% (p=0.002).	NA
Homer 2009	Group versus individual education	Rheumatoid arthritis	Nurse	12 months	Pill counts, at follow-up: 90% adherence among group vs. 69% among individual counseling (p=0.06) Self-reported adherence, at follow up: 97% in group vs. 94% among individual counseling (p=1.0) DMARD use among individual counseling group decreased from 63% at 4 months to 38% at 12 months; decreased among group counseling from 73% at 4 months to 47% at 12 months (p=0.42, NS at 4 months; p=0.61, NS at 12 months)	Patient satisfaction: NS
Nielsen 2010	Group-based educational program	Osteoporosis	Multi-disciplinary team	3,12, and 24 months Adherence at 24 months	IG: 100% self-reported adherence at baseline decreased to 92% CG: 100% adherence decreased to 80% Significantly higher adherence among IG (p<0.006)	Patient knowledge: Increase (+)
Park 2010	Employer-based education program with telephone follow-up	Asthma	Care managers	6 months	NA	Adherence barriers: Decrease (+) Asthma control: Increase (+) Days of work limited by asthma, days that activities were missed or limited: Decrease (+)

Rudd 2009	Education to reduce literacy barriers, enhance health outcomes, and increase self-efficacy	Inflammatory arthritis	Arthritis educator	6 and 12 months	Adherence through 4-item measure on Levine questionnaire: IG: 0.40 (SD, 0.40) adherence decreased to 0.17 (SD, 0.25) at one year; 12.21% decrease CG: 0.30 (SD, 0.37) adherence decreased to 0.18 (SD, 0.30) at one year -- 3.12% decrease	CO (mental health score): Decrease (+) Self-efficacy, satisfaction with care: NS Appointment keeping: NS
Education and behavioral support						
Bocchi 2008	Repetitive education and telephone monitoring	Heart failure	Care team	Mean follow-up=2.47 years	NA	Mortality: NS Unplanned hospitalizations, days of hospitalization, emergency care: Decrease (+)
Edworthy 2007	Comprehensive program including education and self-monitoring	Cardiovascular disease	Care team	19 months	At 19 months of follow-up: ACEIs: 92% among IG vs. 91% among CG (p=NS) Beta-blockers: 89% among IG vs. 80% among CG (p<0.01) ASA: 92% among IG vs. 89% among CG (p=NS) Lipid-lowering agents: 83% among IG vs. 78% among CG (p<0.05) Warfarin: 97% among IG vs. 97% among CG (p=NS)	Re-hospitalization, hospital days: NS Crude mortality: NS
Hacihasanoglu 2011	Patient-oriented education on healthy lifestyle and medication adherence and in-home monitoring	Hypertension	Nursing	6 months	NA	CO (BP): Decrease (+) Health-promoting lifestyle scores: Increase (+) Medication adherence self-efficacy (MASE): <ul style="list-style-type: none"> Group A (general & med adherence education, clinic & home visits) - MASE: 55.3 increased to 71.1 Group B (Group A interventions plus healthy lifestyle behavior education) - MASE: 55.55 increased to 72.27 Group C (Usual care) - MASE: 55.12 increased to 56.85 p<0.005 at post-test (test among three groups) *MASEs: medication adherence efficacy scale; 26-item questionnaire with range of scores from 26 (low) to 78 (high)

Janson 2009	Self-management education on long-term adherence	Asthma	Nurse, respiratory therapist	14 weeks	<ul style="list-style-type: none"> IG: 82% adherence at baseline decreased to 77% after 14 weeks CG: 80% adherence at baseline decreased to 73% at 14 weeks <p>IG 9-times greater odds than CG of more than 60% adherence (p=0.02)</p> <p>Mean adherence decreased over time in both groups although decline was less in IG (p=NS)</p>	Perceived asthma control: Increase (+)
McCarthy 2013	Providing prescription information or services to ED patients; three intervention groups: (1) practical services to reduce barriers to prescription filling; (2) consumer drug information from MedlinePlus; or (3) both services and information	Emergency care	Researcher	1 week	<p>Overall 88% primary adherence by self-report:</p> <ul style="list-style-type: none"> CG: 87% Practical group: 88% MedLine group: 87% Combination group: 88% <p>No clinically meaningful differences in primary adherence by drug class, by whether the drug was prescribed as needed, or by over-the-counter status or by whether the drugs treated an underlying condition.</p>	NA
Moshkovsk a 2011	Multi-faceted intervention, including educational and motivational components plus options including simplified dosing regimens and practical reminders	Ulcerative colitis (5-ASA therapy)	Researcher	48 weeks	<p>Baseline adherence (measured through urine concentration) overall: 76%</p> <p>Baseline adherence of 80% among IG vs. 71% among UC (p=0.30)</p> <p>Follow-up adherence at 48 weeks 76% among IC vs. 32% among UC (p=0.0001)</p>	Patient satisfaction with information: Increase (+)
Wu 2012	Education intervention including Medication Event Monitoring System (MEMs) feedback	Heart failure	Research staff	9 months	<p>3 groups (education and MEMs feedback, education only, usual care):</p> <p>Baseline adherence (defined as rate at or above 88%):</p> <ul style="list-style-type: none"> Education & MEMs group: 70% Education only: 59% CG: 64% <p>(p=0.694 at baseline between groups)</p> <p>At 9 months:</p> <ul style="list-style-type: none"> Education & MEMs: 74% Education only: 65% CG: 36% <p>(p=0.15)</p>	Cardiac event-free survival: Increase (+)
Education and social support						

Chen 2010	Self-efficacy intervention program delivered through DVD, education booklet, and support group	Asthma	Care team, social support	6 weeks	Significant improvement in medication adherence behaviors among patients who received self-efficacy intervention ($p = .008$)	Self-efficacy: Increase (+) Self-monitoring: Increase (+) Follow-up visits: Increase (+) Regular exercise: Increase (+) Asthma attack prevention and management: Increase (+)
Pearce 2008	Practice-based educational intervention to foster involvement of a relative or friend for the reduction of cardiovascular risk	Diabetes	Study personnel, support person	9 or 12 months	<ul style="list-style-type: none"> Group A (pure intervention): 50% high adherence; 42% medium adherence Group B (intervention plus more data collection to explore mechanism of action): 29.8% high; 63.2% medium Group A & B combined: 39.3% high; 53.3% medium Group C (control): 41.8% high; 49.5% medium <p>p (A vs. B. vs. C)=0.1584 p (AB vs. C) = 0.4358</p>	CO (SBP, HbA1C): NS HRQoL: NS Patient satisfaction: NS Perceived health competence: NS
Pladevall 2010	Educational information, pill counts, and designation of a family member to support adherence behavior	Hypertension	Physician, social support	Total study time was 5 years (mean = 39 months); adherence measured at 6 months	<ul style="list-style-type: none"> IG: 61% adherence at baseline increased to 92.2% adherence ($p=0.002$) CG: 69% adherence at baseline increased to 89% adherent at 6 months <p>IG more likely than CG to be at least 80% adherent over 6 month period (OR=1.91; 95% CI: 1.19-3.05)</p>	CO (SBP): Decrease (+) 5-year mortality: NS
Education (counseling)						
Adie 2010	Motivational interviewing and telephone counseling that targeted participant-specific goals related to lifestyle change	Hypertension	Researcher	6 months	Overall increase from 75% taking a statin medication to 84% at 6 months ($p=0.02$)	CO (SBP): NS CO (Cholesterol): Decrease (+) Medication knowledge: Increase (+) Number of BP medications: NS
Perahia 2008	Telephone adherence support intervention	Depression	Health care professional	12 weeks	At study close, IG adherence of 92.6% vs. CG adherence of 92.1%	CO (depression remission): NS Efficacy measures: NS
Taitel 2012	Community-based pharmacist-led face-to-face counseling among new statin users	Statin use	Pharmacist	12 month	<ul style="list-style-type: none"> IG: 87.6% MPR at 2 months decreased to 63.5% at 12 months CG: 84.8% MPR decreased to 58.9% at 12 months <p>IG had significantly higher MPR than CG at end ($p<0.01$)</p>	NA
Education (health coaching)						

Ho 2012	Face-to-face communication skills training	Complementary or alternative medications (CAM)	Researcher	2 physician visits	NA	Discussion of CAM with physician: Increase (+)
Wolever 2010	Integrative health coaching to create an individualized vision of health, goals chosen to align with patient values	Diabetes	Health coach	6 months	Adherence measured using Morisky scale: <ul style="list-style-type: none"> IG: 6.7 (0.96) at baseline increased to 7.2 (0.97) ($p=0.004$ for change over time) CG: 6.7 (1.25) at baseline increased to 6.9 (1.25) (change over time NS) Difference in adherence among IG and CG at 6 months NS	CO (A1C): Decrease (+) Barriers to adherence: Decrease (+) Patient activation, perceived social support, and benefit finding: Increase (+) Exercise frequency, stress, perceived health status: Decrease (+)
Education (motivational interviewing)						
Finocchiaro-Kessler 2012	Motivational interviewing and modified directly-observed therapy (DOT)	Antiretroviral medication use	Nurse	48 weeks	NA	Knowledge: Increase (+)
Rubak 2011	Motivational interviewing	Diabetes	Physician	1 year	No difference between prescriptions written and filled for blood glucose lowering, BP, or lipid lowering medications among IG and CG Significant improvement in adherence among both groups from baseline to one year; nearly 100% adherence in both groups at one year	CO (HbA1C): Decrease (+)
Education (with feedback of clinical values, involving patients in self-monitoring, or e-health)						
Delmas 2007	Physician education and reinforcement using feedback of bone turnover markers	Osteoporosis	Physician	1 year	Medication persistence: higher among those with positive clinical values; changes in adherence NS for stable or poor clinical values One-year persistence through electronic monitoring: 80% among IG versus 77% among UC ($p=0.160$)	CO (new fractures): Decrease (+)
Nassaralla 2009	Education to improve patient participation in medication reconciliation and performance feedback and training to health care team	Primary care	Health care team	Follow-up: 1 month	NA	Completeness and correctness of medication lists: Increase (+)
Neafsey 2011	E-health tailored education program	Hypertension	Nurse	4 months (4 visits; one per month)	NA	Patient knowledge/self-efficacy: Increase (+) Patient satisfaction with care: Increase (+) Treatment intensification: + (lower need for intensification among intervention group)

IG = intervention group

CG = control group

NA = not applicable

UC = usual care
DMARDs = disease-modifying anti-rheumatic drugs
NS = result not significant
+ = statistically significant positive change in outcome
SD = standard deviation
CO = clinical outcomes
ASA = aspirin
MA = medication adherence
BP = blood pressure
SBP = systolic blood pressure
HRQoL = health-related quality of life
MPR = medication possession ratio

Table 2. Augmented pharmacy services interventions to improve patient-centered medication management.

Study	Intervention description	Clinical area	Intervention agent	Duration of follow-up	Evidence for medication adherence outcomes	Evidence for non-adherence outcomes
Calvert 2012	In-hospital counseling, attention to adherence barriers, communication of discharge medications, inclusion of community pharmacist in continued monitoring	Coronary heart disease - aspirin, beta-blockers, and statin use	Pharmacist, with feedback to physician	6 months	Adherence self-report (aspirin, beta blocker & statin) at 6 months: 91% in IG vs 94% in CG (p=0.50) Refill records (beta-blockers & statins): IG 53% vs. CG 38% (p=0.11)	NA
Elliott 2008	Pharmacist telephone follow-up and advice	Chronic disease (diagnosis of cardiovascular disease, diabetes, asthma, or rheumatoid arthritis)	Pharmacist	4 weeks	Non-adherence: 9% among IG vs. 16% among CG (p<0.05)	Medication-related problems: Decrease (+) Mean patient costs: Decrease (+) Less costly, more efficient
Eussen 2010	Pharmacy-based care program to educate patients about importance of medication adherence and association between adherence and clinical outcomes	Statin use	Pharmacist	12 months	<ul style="list-style-type: none"> At 6 months: 11% of IG and 16% of CG had discontinued At one year: 23% discontinuation among IG vs. 26% among CG (HR 0.84, 95% CI: 0.65-1.10, p=NS) One-year MPR: 99.5% among IG vs. 99.2% among CG (p=0.14) 	CO (Total cholesterol): Decrease (+) CO (LDL cholesterol): Decrease (+)
Hunt 2008	Active management by pharmacists in the primary care setting	Hypertension	Pharmacist	12 months	<ul style="list-style-type: none"> IG: 61% in self-reported high adherence group at baseline; increased to 67% at end (p=0.08) CG: No increase in adherence over study (p=0.52) At one year: 67% in IG report high adherence vs. 69% in CG (p=0.77) 	CO (BP): Decrease (+) Knowledge: NS QoL: NS Satisfaction: NS
Klein 2009	Enhanced pharmaceutical care program	Liver transplantation	Pharmacist	12 months	90% dosing compliance among IG vs. 81% among usual care (p=0.015)	CO (Target blood levels): Decrease (+)
Lenaghan 207	Home-based pharmacist medication review with feedback to physician	Elderly taking 4+ medications	Pharmacist, with feedback to physician	6 months	NA	Hospital or care home admissions: NS Mortality: NS QoL: NS Fewer medications in IG

Monte 2009	Clinical pharmacy education, clinical assessment, provider recommendations and follow-up	Diabetes	Pharmacist	1 year	NA	CO (glycosolated hemoglobin, fasting glucose): Decrease (+) CO (BMI, HDL cholesterol, LDL cholesterol, Total cholesterol): NS Costs: NS
Moore 2013	Medication therapy management program	Chronic disease (including asthma, diabetes, heart failure, or heart disease)	Pharmacist	One year	Condition-specific changes in MPR %: Hypertension: IG 2.29 vs CG -2.31 (p<0.001) Dyslipidemia: IG 2.10 vs CG -2.61 (p<0.001) Diabetes: IG 1.64 vs CG -0.73 (p=0.112) Depression: IG 1.23 vs CG 0.07 (p=0.420) Asthma: IG 2.33 vs CG 1.71 (p=0.739)	Plan-paid health care costs: Decrease (+) Hospitalization: Decrease (+) Emergency room visits: NS ROI: Increase (+)
Phumipamorn 2008	Extended pharmacy services including education on appropriate lifestyles and correct diet with pamphlet outlining disease complications, targets of treatment, lifestyle changes, and medications	Diabetes	Pharmacist	8 months	Percent pill count: • IG: 81.8% pill count increased to 88.6%; mean difference 6.8% (p=0.005) • CG: 87.2% pill count decreased to 84.4%; mean difference -2.8% (p=0.29) Baseline within-group percent pill count difference significant (p=0.05) Between-groups percent pill count mean difference significant (p=0.004)	CO (A1C): NS CO (Cholesterol): Decrease (+) Diabetic knowledge scores: Increase (+)
Pindolia 2009	Medication management therapy program	Medicare patients with selected chronic diseases, at least 2 prescriptions, and high annual prescription drug costs	Pharmacist	12 months	ACE/ARB: 10% increase among IG (MTM); 1% decrease among CG (i.e., patients who declined MTM) Beta-blocker: 2% decrease among IG; 8% decrease among CG	CO (GI bleed): Decrease (+) CO (LDL in coronary artery disease, HbA1c values < 7% in diabetes): Trend towards decrease (+) Patient cost: Decrease (+)
Shimp 2012	Medication therapy management program that incorporated medication action plan to incorporate patient preferences for problem resolution	Multiple comorbid conditions	Pharmacist	4 months, 12 months	Baseline MPR for IG and CG: Range 84-96% No significant changes over time for IG or CG	Drug cost: Decrease (+)
Welch 2009	Medication therapy management program for home-based Medicare beneficiaries	Medicare beneficiaries with chronic disease, high medication costs and utilization	Pharmacist	180 days	NA	Mortality: Decrease (+) Hospitalization: Increase (-) Medication costs: Higher cost (-)

IG = intervention group

CG = control group

NA = not applicable
+ = significant positive change in outcome
NS = result not significant
SD = standard deviation
CO = clinical outcomes
MPR = medication possession ratio
BP = blood pressure
QoL = quality of life
BMI = body mass index
ROI = return on investment
ACE = angiotensin-converting-enzyme inhibitor
ARB = angiotensin receptor blockers
MTM = medication therapy management

Table 3. Decision aids and shared decision-making interventions to improve patient-centered medication management.

Study	Intervention description	Clinical area	Intervention agent	Duration of follow-up	Evidence for medication adherence outcomes	Evidence for non-adherence outcomes
Decision aids						
Fagerlin 2010	Decision aid to impact knowledge and attitudes towards tamoxifen use	Breast cancer	Physician	Immediate	NA	Understanding of risks & benefits: Increase (+) Initiation of therapy: NS
Kasper 2008	Patient decision aid	Multiple sclerosis	Physician	6 months	NA	Concordance of roles: NS Treatment choice: NS
Mann 2009	Statin Choice decision aid	Statin use among diabetic patients	Physician	3 and 6 months	80% of participants reported good adherence at 6 months (p=NS between groups)	Understanding of risk (with or without statin use): Increase (+)
Montori 2011	Osteoporosis Choice decision aid	Osteoporosis	Physician	6 months	<ul style="list-style-type: none"> 44% of IG received bisphosphonate at baseline vs. 40% of CG 100% of IG had > 80% adherence at 6 months compared to 74% of CG (p=0.009) 	Understanding of risk: Increase (+) Patient involvement: Increase (+)
Mullan 2009	Diabetes Medication Choice aid	Diabetes	Physician	6 months	<p>Adherence self-report after decision aid: 76% among IG vs. 81% among CG [95% CI: 0.74(0.24 to 2.32)]</p> <p>Persistence & days covered: significantly lower in IG</p>	CO (HbA1c): NS Patient knowledge, involvement: Increase (+)
Thomson 2007	Computerized decision aid to assist with decision to take warfarin or aspirin therapy	Atrial fibrillation and anti-thrombotic therapy	HIT	3 months	NA	CO: NS Decisional conflict: Decrease (+) Care services: NS
Shared decision-making						
Deinzer 2009	Shared decision-making versus patient education for patient empowerment	Hypertension	Physician	1 year	NA	CO (BP): NS
Loh 2007	Multi-faceted program including physician training, a decision board for use during the consultation, and printed patient information	Depression	Care team	6-8 weeks	Medication adherence rate: NS	CO (Depression severity): NS Patient participation, patient involvement: Increase (+) Patient satisfaction: Increase (+) Consultation time: NS

Wilson 2010	Shared decision-making (SDM) versus clinician decision-making (CDM)	Asthma	Physician	2 years	<p>Refill adherence measured as continuous medication acquisition (CMA) = total days supplied divided by 365 days</p> <p>Pre-randomization: 22.2% acquired LABA at least once, 11% acquired an ICS-LABA combo</p> <p>At 2 year: SDM (shared decision-making) had CMA=0.52; CDM (clinician decision-making) had CMA=0.43 (p=0.0346, compare with SDM); CG had CMA=0.42 (p=0.0296, compare with SDM)</p>	<p>CO (health care use, rescue medication use): Decrease (+) CO (lung function): Increase (+) Asthma control: Increase (+) Asthma-related QoL: Increase (+)</p>
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NA = not applicable

+ = significant positive change in outcome

NS = non-significant

IG = intervention group

CG = control group

CO = clinical outcomes

BP = blood pressure

LABA = long-acting beta agonists

ICS-LABA = inhaled corticosteroid/long-acting beta agonist

QoL = quality of life

CMA = continuous medication acquisition

Table 4. Additional interventions to improve patient-centered medication management.

Study	Intervention description	Clinical area	Intervention agent	Duration of follow-up	Evidence for medication adherence outcomes	Evidence for non-adherence outcomes
Case management						
Bogner 2012	Integrated care management to offer education and guideline-based recommendations	Primary care	Care managers, physicians	12 weeks	<ul style="list-style-type: none"> IG: Improved oral hypoglycemic adherence from 35.9% with >80% adherence to 65% CG: decreased from 42% to 31% ($p<0.001$) 	CO (HbA1C): Decrease (+) CO (Depression remission): Increase (+)
Chimbanrai 2008	Involving health care provider and patient to improve adherence, including monthly visits and directly-observed therapy	Tuberculosis	Care team, social support	6 months	NA	CO (rate of cure): Increase (+) Patient knowledge: Increase (+)
Gelmanova 2011	Care team, home visits, and directly-observed therapy	Tuberculosis	Care team	Median program time: 245 days (IQR 147-345)	Baseline adherence of 52% increased to 81%; 56% increase in dosing compliance	NA
Gensichen 2009	Structured telephone interview to monitor disease symptoms and support medication adherence, with feedback to physician	Depression	Health care assistant feedback to physician	12 months	12-month Morisky score of 2.7 among IG vs. 2.53 among CG (mean difference 0.17) ($p=0.042$)	CO (Depression symptoms): Decrease (+) QoL: NS
Hudson 2008	Communication and follow-up to identify barriers to adherence with follow-up to tailor strategies to overcome barriers	Schizophrenia	Nurse	6 months	<ul style="list-style-type: none"> CG (Basic education) baseline adherence increased from 45.5% to 60.6% IG (Enhanced education) increased from 42.8% at baseline to 65.3% at follow-up <p>At baseline, no difference between groups ($p=0.667$); at follow-up: OR=1.94 (95% CI=1.08 to 3.48)</p>	NA
Olsson 2012	Two interventions: (1) home visit by study nurse; (2) home visits and letter with prescription review sent to physician; and (3) nurse home visits, prescription review to physician and a current and comprehensive medication record sent to patient	Primary care	Nurse	12 months	NA	Prescription quality: NS QoL, HRQoL: NS Polypharmacy: NS
Stanhope 2013	Person-centered planning, including extensive counseling and monitoring, documentation of patient personal goals, and the development of service plans and strategies to meet patient goals	Mental health	Physician	11 months	<ul style="list-style-type: none"> IG: adherence increased by 2% per month over the 11-month period ($B=.022$, $p<.01$). CG: No significant change in rate of adherence ($B=.004$, $p<.25$) <p>At 11 months, the rate of adherence for the CG lower than IG.</p>	Appointment-keeping: Increase (+)

					Rate of change in medication adherence for IG and CG differed significantly ($p < .01$).	
Wakefield 2011	Nurse-managed home telehealth intervention	Diabetes and hypertension	Nurse, HIT	12 month	No adherence numbers reported. Authors reported that there was no significant difference between IG and CG.	CO (A1C): NS CO (SBP): Decrease (+)
Feedback interventions						
Chang 2012	Feedback of patient-reported disease severity to physicians	Depression	Physician	3 months	NA	Treatment modification: NS
Christensen 2010	Electronic reminder and monitoring device	Hypertension	HIT	12 months	Self-reported compliance: <ul style="list-style-type: none"> At 6 months, IG (group 1) at 90.6% vs. CG (group 2) at 85.1% (NS) At 12 months, IG (group 2) at 86.3% vs. CG (group 1) at 88.4% (NS) 	CO (BP): NS
Rinfret 2009	Information technology-supported management program and feedback between patients and primary care providers	Hypertension	HIT feedback to physician	12 months	Adherence composite index (continuous medication availability (CMA) times no of anti-hypertension drugs): 1.36 in IG vs. 1.00 in CG at 12 months ($p = 0.008$)	CO (BP): Decrease (+) Dose adjustment: Increase (+) More antihypertensive meds at end of study.
Simon 2011	Online messaging to provide monitoring and counseling for care management	Depression	HIT	4 months; 90 days for adherence	Number (%) using an antidepressant for over 90 days: 81% among IG vs. 61% among CG ($p = 0.001$) Number receiving an additional antidepressant: 22% among IG vs. 16% among CG ($p = 0.27$)	CO (depression scores): Decrease (+) Satisfaction with care: Increase (+)
Wilder 2010	Advanced directive to determine patient preferences and treatment choice	Psychiatry	Physician	12 months	Receiving at least one requested medication predicted greater adherence at 12 months (OR: 7.8, 1.8-34.0, $p < 0.01$).	Concordance between patient preference and prescribing: Increase (+)

IG = intervention group

CG = control group

+ = significant positive change in outcome

CO = clinical outcomes

NA = not applicable

QoL = quality of life

NS = non-significant

HRQoL = health-related quality of life

SBP = systolic blood pressure

HIT = health information technology

Appendix 1. Key terms used in Medline and PubMed searches.

Study Type	Prescriptions Drugs	Patient-centeredness	Outcomes
Clinical trial	Medication, medicine	Shared/sharing and decision-making/ decision-making/choice/behavior	Medication/treatment adherence, compliance, noncompliance, persistence, concordance/Commitment/dose reduction/ discontinuation
Controlled trial, randomized controlled trial	Drug	Decision aid	
Evaluation	Treatment	Patient participation, involvement	Patient participation, involvement
Pretest, posttest	Therapy	Patient preference/feedback/engagement, empowerment/goal/barrier/perspective	Choice/behavior
Time series	Regimen		Patient preference/feedback/engagement, empowerment/goal/barrier/perspective
Intervention	Drug utilization	Person/client/patient- centered/focused/oriented	
Before and after	Prescriptions /prescribing		
	Pharmacy		